DISCUSSION ON THE NEURONE DOCTRINE IN ITS RELATIONSHIP TO DISEASE OF THE NERVOUS SYSTEM.

(Continued from page 514.)

THE FUNCTIONAL SIGNIFICANCE OF THE SIZE AND SHAPE OF THE NEURONE.

Henry H. Donaldson.

Abstract.

These observations were made upon growing nerve cells in the white rat, as they appear between birth and maturity. In the growing spinal ganglion of the lumbar nerves, the increase in volume of the largest ganglion cell-bodies was shown to be very closely correlated with the increase in the area of a cross section of the nerve fiber growing out of these cell-bodies. The examination of the fibers was made on the peripheral side of the ganglion.

Further study of the cross section of the nerve fiber showed that the area of the axis cylinder was almost exactly equal to the area of the surrounding medullary sheath. This held true from the time that the medullary sheath was completely formed on the largest fibers of the sciatic nerve.

In the new-born rat, the sciatic fibers are totally unmedullated, and there is a short preliminary period in which not only the axis cylinder increases, but the medullary sheath is added, and so rapid is this first formation of the sheath that in a few days it attains the relation just mentioned. The relations just mentioned are shown in the table which follows:

WHITE RAT.

	Ratios.		
Body Weight. Grams.	Volumes Ganglion Cells.	Areas Axis.	Areas Axis and Sheath.
4.7	1.0	1.0	1.0
10.4	1.6	1.4	2.8
25.7	4.9	4.6	9.3
68.5	11.2	12.2	24.0
159.0	15.0	14.4	29.7

This equality in the areas of the sheath and axis persists through the entire growing period of the white rat. There are thus two phases in the growth of the medullary sheath, represented first by its rapid appearance, and second by its subsequent slow enlargement. It was shown from the data of comparative anatomy that the *length* of the nerve fiber from a given cell was not correlated with the volume of the cell-body, and was apparently a matter of small significance; the increased length of the fiber not putting a direct nutritional tax on the cell-body itself.

In this connection, the observations of Dr. Elizabeth Dunn were also presented. These showed that the current dictum that the nerve fibers of larger caliber had the longer course did not hold true in the case of the nerve fibers supplying the thigh of the frog, where it could be demonstrated that the average diameter of the fibers innervating the thigh was greater than the average diameter of the fibers passing beyond the knee, to innervate the remainder of the leg. Moreover, the branches going to the thigh contained the very largest fibers that are found in the sciatic nerve.

This statement applies to the several physiological classes of fibers, taken all together, and does not distinguish between the afferent and efferent axones.

Finally, an interpretation of the caliber of the nerve fiber was attempted, and it was pointed out that fibers of large caliber tended to have an extensive terminal distribution. Where the nerve elements were few in number, as compared with the mass of skin or muscle to be supplied, this indicated a coarse innervation. If, however, the number as well as the size of nerve elements was large, a very fine degree of innervation might result, as in the case of the extrinsic muscles of the eye.

DISCUSSION.

Dr. J. J. Putnam said that there was one point that had not been brought out, which is perhaps a corollary from what had been said, namely, that we should modify, if not abandon, the notion that the cell-body has in any special sense the function of storage of impressions. If the cell-body is a network or meeting-place of fibrils, as has been urged, that view of its function is more probably correct which assumes that when any part of the brain is active a series of thrills passes through its component fibers from end to end, and the assumed "storage" should rather be rendered as changes in co-ordination. The sensori-motor mechanism acts as a whole, and there is no storage in the cells, which are rather "nodal points."

Dr. F. W. Langdon thought that to begin at this date to criticise the neurone doctrine is very much like criticising the utility of a building of which the plans are not yet drawn. We have all realized the truth of the saying that facts are stubborn things. He thought we ought also to remember that they are not only stubborn, but exceedingly *useless* things until connected by something in the nature of theory or hypothesis, and, we may safely say, with regard to the neurone doctrine, that anatomically it has helped us to convert, perhaps, what was but a jungle or wilderness of foliage into something resembling an orderly garden of shrubbery and classified plants.

Pathologically it has enabled us to collect together a large number of otherwise disconnected and useless facts, which we have, in some measure, converted into a pathological mosaic of considerable practical value.

Clinically, we were very much in the position with respect to the nervous system before the announcement of the neurone doctrine that the hematologist would have been before the discovery of the blood corpuscles. How would he have differentiated between the anemias? Therefore, to criticise at this early date the neurone doctrine as not leading to radical results in treatment is a little premature. It is our imperfect knowledge of the details of the neurone doctrine, not the principle itself, which is at fault. Even in this imperfect state the neurone doctrine has led not only to practical advances in anatomy, physiology and pathology, but also, by reason of furnishing a clearer basis for thought, to better results in diagnosis and prognosis; and it cannot fail to lead eventually to a more rational treatment of nervous diseases. If a man can think clearly he is more likely to intelligently treat a disease than if he argues from a disconnected mass of facts, as we formerly did. Dr. Langdon wished to go on record, therefore, as being firmly convinced of the great importance of the doctrine in a practical as well as in a theoretical sense.

Dr. Van Gieson said so much had been given in the symposium on the neurone theory that it was difficult to attempt any adequate discussion. We ought all of us to acknowledge our indebtedness to the first speaker for bringing together in his work on the nervous system in book form the scattered facts and theories of the neurone doctrine which have accumulated in the vast literature of the past decade. Works like those of the first speaker which bring together desultory facts and observations upon the neurone into a coherent whole, thereby giving an opportunity for viewing the interdependence and relationship of these facts are fully as important as the individual observations and discoveries, and indeed more valuable.

At the same time Dr. Van Gieson did not know that the neurone doctrine at this late day needed so strong a defense. The neurone doctrine now has become universal and valid knowledge; it is accepted as a well-grounded scientific principle, founded on an enormous supply of inductive data. The establishment of the neurone theory is overwhelming and to combat the older views, or a few recently found facts which seem to speak against the doctrine, seems like slaying the slain and vanquishing what is already defeated. The neurone doctrine is the extension of the universal cellular structure of tissues in general to the nervous system, and His in 1879 brought out this view in demonstrating that each axone was the outgrowth and dependency of the corresponding neurone cell-body. Quite true, it is not so long ago that students obtained the impression from such a text-book as Gray's Anatomy that nerve fibers were one thing and ganglion cells another. Dr. Van Gieson felt that all of us who have occasion to teach the anatomy or functions of the nervous system begin with the neurone doctrine as soon as possible and consider that the former views merely have a historical interest. What is there, then, that speaks against the neurone theory? He could not see how concrescence of neurones gives the slightest basis to doubt the validity of the neurone doctrine, or the primary character of the neurones as individual cells. We might as well question the individual character of the stellate branching cells in myxomatous tissue, because they anastomose, or any other cell which has intercellular bridges or anastomoses. This question of neurone concrescence in whatever character it appears is a secondary modification dependent upon the fixed nature of the function of the annectant neurones. Nor could Dr. Van Gieson see how the exposition of the neurone fibrils gives us the barest foundation to doubt the neurone theory and that the neurones are primarily individual cells.

In regard to the splendid array of facts brought out by the second speaker the suggestion may perhaps be timely that we shall not be able to understand all these morphological data of the neurone until we devote more attention in connection with structural data to the function and physiology of the neurone. If we make use of the parallelism of fluctuation of neurone energy with the succession of psycho-motor phenomena, our interpretation of these phenomena as well as of structural neurone changes is greatly illumined. The rise and fall of the threshold of neurone energy, it seemed to Dr. Van Gieson, is really one of the greatest ideas in interpreting a great host of phenomena in abnormal nervous life. These morphological data are liable to remain in a chaotic condition until we use them in connection with some general guiding principle underlying the phenomena of neurone function.

The third paper at the beginning brings some disappointment to the hopes that ultimately the extension of the neurone doctrine into the domain of abnormal mental and nervous life would bring an increase in our power to cure or control these manipulations. It appears, if Dr. Van Gieson understood the speaker, that from a practical standpoint incurring disease we are not much better off than we were before. This in general may be quite true, but we need not be discouraged at the slow fulfilment of gain in practical treatment born of the neurone theory. We have hardly begun to apply the neurone theory. Dr. Van Gieson meant more especially the physiological neurone theory and not the morphological theory—to unravel the succession of morbid nervous and mental phenomena. But the extension of the doctrine into this field is sure to revolutionize our whole conception of clinical neurology and psychiatry. While it is quite true that some stages of the dissipation of neurone energy are beyond restitution, one thing is sure, and that is, that we cannot handle a mechanism until we understand it; we cannot lay hold of phenomena until we know their succession, and can forecast them. To work out the succession of phenomena the establishment of laws and theories are requisite. This being the case, we are somewhat surprised to hear the speaker sound a note of warning that theory after theory is being piled up on the neurone conception. We can have no ultimate progress of the neurone doctrine in the treatment of nervous and mental diseases without these theories. Far from being a disadvantage, calling for rebuke, these theories are, on the contrary, of the greatest help. Facts without theories is chaos. We need fear no apprehension about the growth of theories of the neurone principle. The inadequate ones in the course of time will be weeded out and do no harm, while the broader theories which stand the test of verification will undergo the selection of the fittest and eventually stay and become valid knowledge. For his part, he had had occasion to witness the direct outcome of the neurone doctrine in actual practical cures of the most signal importance, in psychopathic functional disease. We are working in this direction all the time and our great guide and mentor are some psychopathological principles, that we have worked out from the neurone conception. As for the retraction theory he was more firmly convinced of its validity than ever. Ameboid motion of the neurones had been mentioned here this morning. We ought to get rid of this term and the idea it conveys. This notion seems to have grown out of Wiedersheim's observations which Dr. Van Gieson felt sure time will prove to be erroneous. There is no such coarse expression of neurone motility as ameboid motion would convey. Only the terminals of the neurones may be supposed to contract and expand, and this indeed to a slight and perhaps almost infinitesimal degree. Two years ago, and again since that time, Dr. Van Gieson had expressed the view that the nervous system is neither made up of concrescent nor free neurones exclusively, but of both. And, to him, it seemed strange to see a sharp line of division established in the discussion of neurone retraction, one school having it that neurones are concrescent, the other that they are retractile. If one would stop to reflect on the subject a little, it would be obvious from the nature of nervous and mental phenomena, both normal and abnormal, that both types of neurones go to make up the nervous system. The field of the microscope is not the place to prove neurone retraction. If he should actually be able to see evidences of neurone retraction under the microscope, it would not add one iota to his belief in its existence, any more than his belief in the molecular theory would depend upon his catching hold of a molecule and holding it in his hand. Neurone attraction we assume, and if it is verified by psychomotor phenomena its proof is just as strong as the verification of the molecular hypothesis by the phenomena of the physical world. The people who demand actual perceptial demonstration of neurone retraction before believing in it seem to forget that the very nature of a hypothesis is such as to transcend the limitations of our perception. Hypotheses are conceptional creations, but always similar to and congruous with our perceptual data.

In fact, while they were ardent champions of the retraction theory as applied to the higher functions of the nervous system, Mr. Weil and Mr. Frank working in the Pathological Institute had shown that the data of the objective demonstration of neurone retraction under the microsope is utterly unreliable. It is the deductive application of neurone attraction that establishes our basis of belief in this theory, and with Dr. Sidis a preliminary argument was presented under the title of "Neurone energy and its psychomotor manifestations" sustaining this view.

The fourth paper is a veritable treasure. Here is the ontogenetic source of data which fit in perfectly with the laws of neurone cytolysis, disaggregation of neurone hierarchies—except that in ontogenetic, and probably also in phylogenetic development, the phenomena are presented in reverse order of those of neurone cytolysis.

Dr. F. X. Dercum said that notwithstanding all that has been said, he did not know of any theory that offered as good a working hypothesis as regards the explanation of mental processes, both normal and pathological, as does the retraction theory. He did not for a moment maintain, however, that actual physical retraction of cell processes is necessary; indeed, he could conceive of the changes consisting of mere physiological interruptions in the relations of the neurones to each other without gross physiological change. However, he thought it is best for us to wait until our knowledge on the subject has been more complete, until we know more about the details of the relations of the neurones to each other in all portions of the nervous system, before attempting a further explanation. He had learned the danger of speculating on unknown grounds. Still a working hypothesis has its value. For instance, no theory of memory that has ever been offered can even approximate that offered by the so-called retraction theory. It is better to wait, however, and the old German adage may still be true—"He who laughs last, laughs best."

Dr. E. B. Angell said that Dr. Barker had touched on one point that we as clinical neurologists have been waiting for, from the laboratory workers of the day, the question of the nutrition of the neurone. We have been too much taken up with the study of the morphological changes of the neurone from a histological standpoint, and while he appreciated the work of Dr. Spiller he thought a great deal can be learned from the study of the influence of circulation upon the changes in the peripheral neurone. In a case he had seen a short time ago an arterio-fibrosis was associated with multiple neuritis affecting the feet. In one foot gangrene had resulted and amputation of the foot had been resorted to. The surgeons had been compelled in turn to amputate the toe, the ankle, and finally the foreleg. The neuritis was not recognized and on account of the arterio-sclerosis the nutrition of the peripheral neurone was faulty, in consequence of which the gangrenous condition reappeared at the higher level.

Dr. Angell suggested large doses of nitro-glycerine, knowing that we could in that way get some dilatation of the fibroid arteries. Nitro-glycerine had been tried, but with insufficient strength. Under the influences of large doses the local nutrition was improved and the patient recovered. The neuritis was in time relieved and the man is well to-day. Such is the clinical evidence of the importance of studying the local nutrition of the terminal neurone, and he believed if some proper methods could be devised by laboratory workers for studying the local circulation much light could be thrown on the changes in the neurones, not only in the terminals of the neurone, but also in the cell-bodies.

Dr. J. J. Putnam said that this differentiation between the cell-process and cell-body which had been referred to by Dr. Spiller is important from a pathological point of view, and also from a physiological point of view. We all remember the interesting experiment of Prof. Bowditch, showing the nerve fiber is incapable of fatigue, whereas the nerve cell is readily fatigued; so that the cell as a whole is a differentiated body, and that lays additional weight to what Dr. Sachs had said, that in dealing with pathological and clinical cases, we should have a record of facts as they are, and not force them to suit anatomical conceptions. We should not forget the debt that we owe to the old notion of "trophic domain," of which Dr. Barker had spoken. The neurone theory has as yet given us little else beyond the reinforcing of this notion that is of practical value in clinical pathology.

Dr. Joseph Collins said that he was somewhat bewildered, as well as very materially instructed, after listening to this discussion. In discussing the neurone doctrine we are not dealing with theories, but with facts, and, in the solution of many of the questions that come up in pathology and in physiology, we are endeavoring to fit pre-conceived theories with the facts of the neurone doctrine. It is always a difficult matter to discuss papers constituting a symposium, because they supply a complete and final discussion from different points of view. We are under obligation to the first speaker for having presented to us in such a clear, succinct, and critical way, this complete digest of the present status of the neurone doctrine. Its value was quickly manifest in the reading of the following papers, pointing out distinctly the necessity of using the term nerve cell as synonymous with neurone, and not speaking of the nerve cell when the cell-body is meant, and other clear distinctions.

Dr. Collins said he had long endeavored to follow Dr. Van Gieson and Dr. Dercum, as they had striven to unravel the contraction theory, and it seemed to him that until something more convincing was forthcoming we should devote no further time to it. Dr. Collins congratulated Dr. Spiller on the amount of pathological and anatomical material which he had been able to bring to corroborate his statements, and to make lucid demonstrations of the tenets which he had held. Dr. Sachs, he said, had taken a somewhat more pessimistic view of the bearing of the neurone theory on the explanation of nervous disease than Dr. Collins was inclined to take, yet he felt in sympathy with much that had been said. Up to the time that the neurone doctrine was brought forward, Dr. Collins had had no consistent and satisfactory idea, as he had now in a measure, of the different forms of progressive muscular atrophy and dystrophy, including amyothrophic lateral sclerosis. But it seemed to him now that he could use his pictorial memory in explaining the various forms of dystrophy and atrophy, whether of the Aran-Duchenne type, or the neural or muscular variety, by the aid of the neurone doctrine.

Dr. L. F. Barker said that in the very interesting series which Dr. Spiller brought forward of partial degenerations of the neurone, he (Dr. Barker) was reminded of the occurrence of partial cell degeneration elsewhere in the body. We can have partial cell necrosis in the liver or kidney cell without causing complete death of the cell.

As to the relation of the pyramidal tract to the ventral horn of the spinal cord the observations of the actual changes in the cell-bodies of the lower motor neurones are extremely interesting. They have a bearing on the question of the exact relation of the upper to the lower motor neurone. Many will recall that von Monakow has maintained that the axones of the pyramidal tract do not come into direct connection with the cell-bodies of the ventral horn cells, but that there is a group of small neurones (Schaltzellen) interposed between the upper motor segment and the lower. It will be interesting to follow these pathological changes and to see whether ultimately we shall have to consider the cortico-muscular conduction path as consisting of two sets of superimposed neurones or of three.

The volume of the axis cylinder of the nerve fiber as compared with that of the nerve cell body had interested Dr. Barker for some time. His attention was first forcibly directed toward it by reading Dr. Donaldson's book on the growth of the brain. It is, if he remembered correctly, in that that he makes the statement that the volume of the axis cylinder may be one hundred and eighty-seven times greater than the volume of the cell-body.

Dr. Barker wished to say that his conception of the neurone was not based on purely morphological grounds, but just as much on physiological and pathological results as upon form relations.

With regard to the relation of the neurone doctrine to the study of disease clinically, he had been glad to hear that clinicians have been as much helped as they have. It was surprising to him that the doctrine should have entered so quickly into clinical thought.

Dr. W. G. Spiller said he had understood Dr. Donaldson to say that in the same animal the axone supplying a distal part of the limb was not larger than that supplying a proximal part, that is, the diameter of a long axone might be smaller than the diameter of a shorter axone. He was not quite sure that he understood Dr. Donaldson's method of determining this fact. Dr. Donaldson had taken the axone of a nerve in the thigh, for example, and found it to be of a certain diameter. It seemed to Dr. Spiller possible that an axone in the thigh may give off collaterals, and that this axone may become smaller as portions lower in the limb of the animal are examined. He had not understood whether Dr. Donaldson took into consideration the distribution of the collaterals from the portion of the axone in the upper part of the limb.

The explanation of atrophy in cerebral disease, Dr. Spiller thought, was very difficult. It has been believed by some to be due to arthritis, by others to alteration in the cells of the anterior horns of the cord, and by others to vascular changes produced by cortical lesions.

Dr. Spiller said that he was becoming more and more skeptical as regards the importance of chromatolysis without other lesions. Chromatolysis is of value in determining the location of the cell-bodies of diseased axones, but as indicative of altered function it has a limited value. The displacement or destruction of the nucleus, the tumefaction of the cell-body, the destruction of the dendritic processes, the alteration of the other contents of the cell-bodies, seemed to him more important that the breaking up of the chromophilic elements, and it has been shown by experimental work that chromatolysis may occur without any disturbance of function having been noted during life.

Dr. Sachs remarked that there was evidently an impression abroad that he was not especially fond of theories. He did not think less of theory, but more of facts. There is a vast difference between a theory and a fancy. The theory must always be developed *pari passu* with the facts. What would we have thought of the Darwinian theory if Darwin had not furnished that stupendous array of facts in support of his teachings no one has been able to deny. Do not let the theory jump ahead of facts, and don't waste time to find the evidence in support of the theory when you can look through the microscope. The evidence must be practical and more spontaneous. Dr. Sachs thought that the neurone theory would do a great deal in the further development of our understanding of the nervous system. If he had seemed pessimistic, it was because he was anxious not to indulge in fanciful pathological discussions.

Dr. H. H. Donaldson said that Schwalbe started with the theory that the largest nerve fibers have the longest course.

He next developed the idea of the conical diminution of the fibers in their course. That was necessary to support the doctrine, because the large nerve fibers were not to be found at the periphery. If they run a long course, then they must disappear on the way. Conical diminution was brought in to account for this disappearance. That is Schwalbe's statement of the situation.

Dr. Donaldson had evidence that in the course of the sciatic nerve, where the branches are given off for the innervation of the thigh, that approximately 6 to 8 per cent. of the fibers given to the branches are the result of division of fibers, one portion of which runs on below the knee and the other stops in the thigh. That the diminution in the average diameter below the knee is due to a conical diminution is met by the observation that in the branches to the thigh the maximal fibers are practically all found. These appear above the point at which the branches leave for the thigh and they appear in the branches which are distributed to the thigh, and thus their course is accounted for through its entire extent.

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108 "UEBER DIE VORÜBERGEHENDEN ZUSTÄNDE ABNORMEN BEWUSSTSEINS IN FOLGE ALKAHOLVERGIFTUNG, UND ÜBER DEREN FORENSICHE BEDEUTUNG" (Transitory Abnormal Conditions of Consciousness Due to Alcohol Poisoning and Their Forensic Indications). Moeli (Allg. Zeitschrift für Psychiatrie, 1900, LVII, 2 & 3, S. 169).

The author makes an important clinical contribution to the study of temporary mental disturbances due to alcohol poisoning. The histories of fourteen cases are studied in detail and their close connection with alcoholic indulgence is shown. It is pretty clearly established that they are not to be regarded as examples of true epilepsy. A number of them developed on an hereditary basis; in others intolerance to alcohol appeared after an accident of some sort. Most of them had been guilty of criminal acts, ranging from simple exhibitions to violent assault and even to murder. The medico-legal points involved are considered at some length by the author. ALLEN.